

This Page Is Inserted by IFW Operations
and is not a part of the Official Record

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

IMAGES ARE BEST AVAILABLE COPY.

**As rescanning documents *will not* correct images,
please do not report the images to the
Image Problem Mailbox.**

REMARKS

Claims 105-161 are currently pending. Claims 105, 106, 108, 109, 113, 114, 122, 124-137, 151, 152, 154 and 161 are rejected, and claims 107, 110-112, 115-121, 123, 138-150, and 155-160 are objected to by the Examiner. Claims 105, 108, 112, 124, 138 and 161 are amended in this response.

Amendments to the Specification

The paragraph under the heading "Cross-Reference to Related Applications" has been amended to include the status of the parent application.

Amendments to the Claims

The structural requirements of the claimed polyamino acid of claim 105 include 2-2000 Z type amino acids, limited to basic amino acids in this claim and linked by peptide bonds. Claim 105 is amended to clarify that the Z groups are linked by Z—Z peptide bonds. Applicant believes that Z—Z bonding is shown in Formula I on page 6 of the specification. Support for this amendment can also be found in Formula VIII on page 19 of the specification.

Claim 108 is similarly amended to recite that the Z groups are linked by Z—Z glycosidic bonds. Support for this amendment can be found in Formula I on page 6 and Formula IX on page 22 of the specification. Claim 108 is also amended to recite that m is 1 at least once in the compound and m is zero at least once in the compound, thus requiring that R is present at least once in the compound. This amendment makes claim 108 consistent with the other claims. Support for this amendment can be found in the specification on page 21, lines 17-31, which discusses lipophilic polycationic polysaccharide compounds of Formula I where R is an alkyl or alkenyl.

Claims 112, 124, and 138 are amended to correct obvious typographical errors. Claim 112 is amended to include the correct spelling of "diethylaminoethyl". The

formula in claim 124 is amended so that the A groups are "A₁" and "A₂". Claim 138 is amended to correct the spelling of the word "monosaccharides". Applicant thanks the Examiner for identifying these typographical errors.

Claim 161 is amended to recite that R_A is an alkyl or alkenyl having from about 12 to about 22 carbon atoms. Support for this amendment can be found on page 19, lines 15-20, which discusses lipophilic polyamino acids with long hydrocarbon chains. Additional support for this amendment can be found on page 18, lines 3-6, which discloses other subsets of Formula I where preferred R groups are an alkenyl having about 12 to about 22 carbon atoms. Additional support can be found on page 51, Scheme 12, which discloses the polysaccharide subset of Formula I where R₂ includes an alkyl or alkenyl having from about 12 to about 22 carbon atoms.

Rejections under 35 U.S.C. 112

The Examiner rejected claims 124-137 under 35 U.S.C. 112, second paragraph, as being indefinite because both A groups in the formula of claim 124 are A₁, which contrasts with the description of the A groups in the remainder of claim 124 wherein the A groups have subscripts of "1" and "2". Claims 125-137 are indefinite as result of depending from claim 124. Claim 124 is presently amended so that the A groups in the formula are A₁ and A₂. As a result of correcting this error, Applicant believes claims 124-137 are allowable.

Rejections under 35 U.S.C. 101 and 102

Claim 105 and its dependent claims 106, 113, 114, and 122 were rejected under 35 U.S.C. 101 and 102 in light of Christensen et al. Christensen et al. discloses fibrillan, which contains dimethylated arginine residues and a lysine residue separated by non-basic amino acid residues. The Examiner alleges that there is no claim limitation in claim 105 that requires the Z moieties, which are limited to basic amino acids, to be contiguous. Fibrillan, a natural product, is therefore encompassed within claim 105. Claim 105 is presently amended to require the Z moieties to be linked by Z—Z peptide

bonds. Christensen et al. does not disclose fibrillan as having two or more adjacent basic amino acids where at least one of the basic amino acids has an R group as defined in claim 105. As presently amended, claim 105 does not encompass any compound disclosed or suggested in Christensen et al. As a result, the rejections under 35 U.S.C. 101 and 102 to claim 105 and its dependent claims should be withdrawn.

Claim 108 and its dependent claims 109, 151, 152, and 154 were rejected under 35 U.S.C. 101 and 102 in light of Lehninger, which discloses α -amylose, maltose, sucrose, and lactose which are all naturally occurring unbranched polysaccharides. Claim 108 is presently amended to recite that the Z groups are connected together by Z—Z glycosidic bonds and that “m” must be 1 at least once in the compound. Claim 108 as presently amended claims a polysaccharide chain having at least one of the R groups recited in the claim attached to a Z monosaccharide. Polysaccharides without side chains falling within the R groups recited in the claim do not fall within the scope of claim 108 as presently amended.

Lehninger also discloses a muropeptide (page 233) comprising a disaccharide having a peptide side chain. The peptide side chain comprises four amino acids including two alanine residues. In claim 108, R is either an alkyl or alkenyl having 12-22 carbon atoms, or R is a steroid selected from the group consisting of stigmasterol, ergosterol, and cholic acid. The Examiner alleges that the peptide side chain of the muropeptide falls within the definition of R in claim 108 because it is an alkyl having 20 carbon atoms. The Examiner states the four amino acid peptide side chain of the muropeptide is an alkyl because the alanine residues contain alkyl groups.

Applicant respectfully disagrees with the Examiner. An alkyl is commonly defined as a hydrocarbon that lacks one of the hydrogen substituents of an alkane (Francis A. Carey, “Organic Chemistry, 2nd Edition” (1992) page 60). An alkane is a hydrocarbon having the general formula C_nH_{2n+2} (Morrison and Boyd, “Organic Chemistry, 4th Edition” (1983) page 87; Francis A. Carey, “Organic Chemistry, 2nd

Edition" (1992) page 51). Although the peptide side chain of the muropeptide contains an alkyl group, the peptide side group as a whole clearly does not fall within the general formula and definition of an alkyl. The rejections to claims 108, 109, 151, 152, and 154 should be withdrawn because Lehninger does not disclose or suggest a polysaccharide having an alkyl or alkenyl having 12 to 22 carbon atoms, or a steroid attached to at least one of the monosaccharide moieties.

Claim 161 was rejected under 35 U.S.C. 101 and 102 in light of the Human adrenocorticotrophin and Bovine ribonuclease disclosed in Lehninger. Claim 161 claims a polyamino acid having an R group attached to at least one of the amino acids, wherein R could be a C₁₋₂₃ alkyl or alkenyl, or a steroid. The Examiner points out that threonine, alanine, and isoleucine are methylated versions of serine, glycine, and valine. Thus, a polyamino acid as disclosed in Lehninger containing a combination of threonine with serine, or alanine with glycine, or isoleucine with valine, meets the structural requirements of claim 161.

Claim 161 is presently amended to recite that R can be an alkyl or alkenyl having from about 12 to about 22 carbon atoms, or a steroid. None of the amino acid residues disclosed in Lehninger contain alkyl or alkenyl side chains having between 12 and 22 carbon atoms, or steroid side chains. Claim 161 as presently amended does not encompass any compound disclosed or suggested in Lehninger. As a result, the rejections under 35 U.S.C. 101 and 102 should be withdrawn.

Informalities and Claim Objections

The disclosure was objected to because of misspellings in claims 112 and 138. Claims 139-150 were objected to because they depend from claim 138. Accordingly, claims 112 and 138 have been corrected.

The Examiner stated that claims 107, 110, 111, 115-121, 123, 153, and 155-160 were objected to as being dependent upon rejected base claims, but would be allowable

if rewritten in independent form. Applicant believes the corresponding base claims are allowable as a result of the amendments and arguments discussed above. Therefore, claims 107, 110, 111, 115-121, 123, 153, and 155-160 should also be allowable.

Conclusion

As a result of the amendments and arguments made above, it is believed that claims 105-161 are in condition for allowance. Copies of pages from Morrison and Boyd, "Organic Chemistry, 4th Edition" (1983), and Francis A. Carey, "Organic Chemistry, 2nd Edition" (1992) are attached to support arguments made above.

It is believed that no fee is required with this submission. If this is incorrect, please charge any required fees to deposit account 07-1969.

Respectfully submitted,

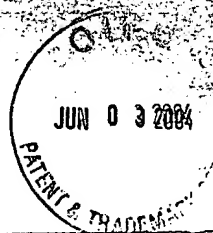
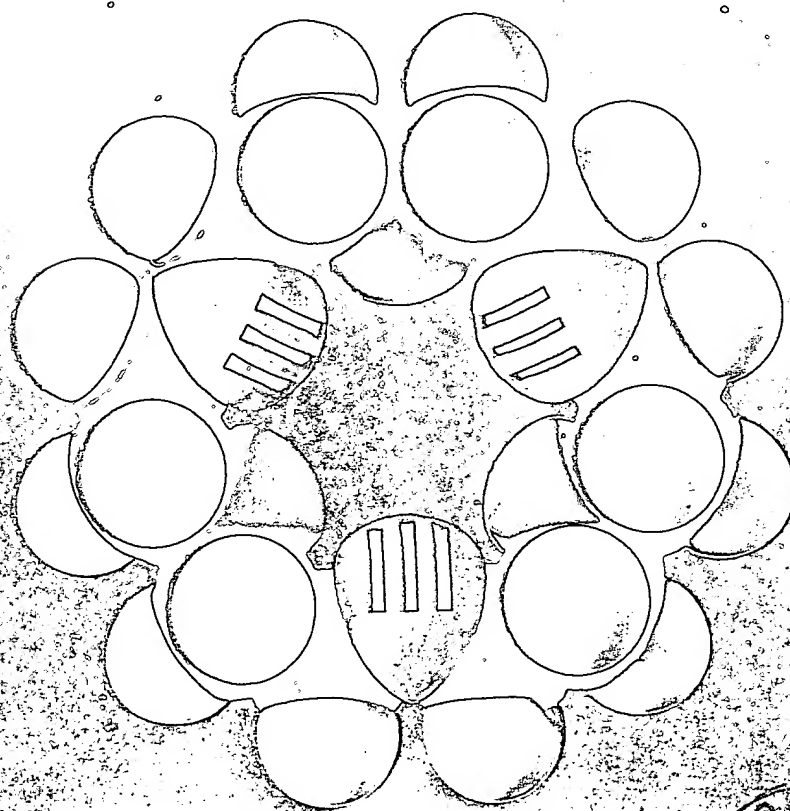


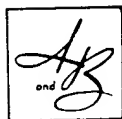
Michael J. Curtis
Reg. No. 54,053
Customer No. 23713

Greenlee, Winner and Sullivan, P.C.
5370 Manhattan Circle, Suite 201, Boulder, CO 80303
Phone: (303) 499-8080; FAX: (303) 499-8089
Email: Winner@Greenwin.com
Attorney Docket No. 45-93A
ks: June 9, 2004

MORRISON
AND BOYD

ORGANIC
CHEMISTRY
FOURTH EDITION





Production supervisor: Judith Fiske
Production Editor: Mary Hill
Cover designers: Vicky Prescott
Christy Rosso

Copyright © 1983, 1973, 1966, 1959 by Allyn and Bacon, Inc., 7 Wells Avenue, Newton, Massachusetts 02159. All rights reserved. No part of the material protected by this copyright notice may be reproduced or utilized in any form or by any means, electronic or mechanical, including photocopying, recording, or by any information storage and retrieval system, without written permission from the copyright owner.

Library of Congress Cataloging in Publication Data

Morrison, Robert Thornton
Organic chemistry.

Bibliography: p. 1293
Includes index.

1. Chemistry, Organic. I. Boyd, Robert Neilson.

II. Title.

QD251.2.M67 1983 547 82-8855
ISBN 0-205-05838-8

Cover photograph: 18-Crown-6

Printed in the United States of America.
10 9 8 7 6 5 4 3 87 86 85 84 83

Preface x
Acknowledgments xi

PART I

The Fundamentals

1. Structure and Properties of Matter

- 1.1 Organic Chemistry
- 1.2 The structure of matter
- 1.3 The chemical bond
- 1.4 Quantum mechanics
- 1.5 Atomic structure
- 1.6 Electromagnetic radiation
- 1.7 Molecular structure
- 1.8 The covalent bond
- 1.9 Hybrid orbitals
- 1.10 Hybridization
- 1.11 Hybridization
- 1.12 Unshared electron pairs
- 1.13 Intramolecular forces
- 1.14 Bond dissociation energy
- 1.15 Polarity
- 1.16 Polarity
- 1.17 Structural isomerism
- 1.18 Melting point
- 1.19 Intermolecular forces
- 1.20 Boiling point
- 1.21 Solubility
- 1.22 Solubility
- 1.23 Acids and bases
- 1.24 Isomerism

2. Methane and the Alkanes

- 2.1 Hydrocarbons
- 2.2 Structural isomerism
- 2.3 Physical properties
- 2.4 Sources
- 2.5 Reactions
- 2.6 Oxidation
- 2.7 Chlorination
- 2.8 Control of pollution

Table 3.2 NAMES OF ALKANES

CH_4	methane	C_9H_{20}	nonane
C_2H_6	ethane	$\text{C}_{10}\text{H}_{22}$	decane
C_3H_8	propane	$\text{C}_{11}\text{H}_{24}$	undecane
C_4H_{10}	butane	$\text{C}_{12}\text{H}_{26}$	dodecane
C_5H_{12}	pentane	$\text{C}_{14}\text{H}_{30}$	tetradecane
C_6H_{14}	hexane	$\text{C}_{16}\text{H}_{34}$	hexadecane
C_7H_{16}	heptane	$\text{C}_{18}\text{H}_{38}$	octadecane
C_8H_{18}	octane	$\text{C}_{20}\text{H}_{42}$	eicosane

The student should certainly memorize the names of at least the first ten alkanes. Having done this, one has at the same time essentially learned the names of the first ten alkenes, alkynes, alcohols, etc., since the names of many families of compounds are closely related. Compare, for example, the names *propane*, *propene*, and *propyne* for the three-carbon alkane, alkene, and alkyne.

But nearly every alkane can have a number of isomeric structures, and there must be an unambiguous name for each of these isomers. The butanes and pentanes are distinguished by the use of prefixes: *n*-butane and *isobutane*; *n*-pentane, *isopentane*, and *neopentane*. But there are 5 hexanes, 9 heptanes, and 75 decanes; it would be difficult to devise, and even more difficult to remember, a different prefix for each of these isomers. It is obvious that some systematic method of naming is needed.

As organic chemistry has developed, several different methods have been devised to name the members of nearly every class of organic compounds; each method was devised when the previously used system had been found inadequate for the growing number of increasingly complex organic compounds. Unfortunately for the student, perhaps, several systems have survived and are in current use. Even if we are content ourselves to use only one system, we still have to understand the names used by other chemists; hence it is necessary for us to learn more than one system of nomenclature. But before we can do this, we must first learn the names of certain organic groups.

3.8 Alkyl groups

In our study of inorganic chemistry, we found it useful to have names for certain groups of atoms that compose only part of a molecule and yet appear many times as a unit. For example, NH_4^+ is called *ammonium*; NO_3^- , *nitrate*; SO_3^{2-} , *sulfite*; and so on.

In a similar way names are given to certain groups that constantly appear as structural units of organic molecules. We have seen that chloromethane, CH_3Cl , is also known as *methyl chloride*. The CH_3 group is called **methyl** wherever it appears, CH_3Br being *methyl bromide*; CH_3I , *methyl iodide*; and CH_3OH , *methyl alcohol*. In an analogous way, the C_2H_5 group is **ethyl**; C_3H_7 , **propyl**; C_4H_9 , **butyl**; and so on.

These groups are named simply by dropping *-ane* from the name of the corresponding alkane and replacing it by *-yl*. They are known collectively as **alkyl groups**. The general formula for an alkyl group is $\text{C}_n\text{H}_{2n+1}$, since it contains one less hydrogen than the parent alkane, $\text{C}_n\text{H}_{2n+2}$.

Among the alkyl groups we again encounter the problem of isomerism. There

ORGANIC CHEMISTRY

SECOND EDITION

FRANCIS A. CAREY

Department of Chemistry
University of Virginia

McGRAW-HILL, INC.

New York	St. Louis	San Francisco	Auckland	Bogotá
Caracas	Lisbon	London	Madrid	Mexico
Montreal	New Delhi	Paris	San Juan	Milan
Sydney	Tokyo	Toronto		Singapore

ORGANIC CHEMISTRY

Copyright © 1992, 1987 by McGraw-Hill, Inc. All rights reserved.
Printed in the United States of America. Except as permitted under the
United States Copyright Act of 1976, no part of this publication may be
reproduced or distributed in any form or by any means, or stored in a data
base or retrieval system, without the prior written permission of the
publisher.

3 4 5 6 7 8 9 0 VNH VNH 9 0 9 8 7 6 5 4 3 2

ISBN 0-07-009934-0

This book was set in Times Roman by Progressive Typographers, Inc.
The editors were Kirk Emry and David A. Damstra;
the designer was Rafael Hernandez;
the production supervisor was Annette Mayeski.
The copy editor was Richard A. Mickey.
The photo researcher was Elyse Rieder.
New drawings were done by J & R Services, Inc.
Von Hoffmann Press, Inc., was printer and binder.

The stamps in the introduction (pp. 1-5) are courtesy of James O. Schreck, professor of chemistry,
University of Northern Colorado.

Library of Congress Cataloging-in-Publication Data

Carey, Francis A., (date).
Organic chemistry / Francis A. Carey. — 2nd ed.
p. cm.
Includes index.
ISBN 0-07-009934-0
1. Chemistry, Organic. I. Title.
QD251.2.C364 1992
547—dc20 91-19188

The ^1H nuclear magnetic resonance spectra are reproduced with permission from "The Aldrich
Library of NMR Spectra," first edition, C. J. Pouchert and J. R. Campbell, the Aldrich Chemical
Company, 1975.

Infrared spectra are reproduced with permission from "The Aldrich Library of FT-IR Spectra," C. J.
Pouchert, the Aldrich Chemical Company, 1985.

The ^{13}C nuclear magnetic resonance spectra are reproduced with permission from "Carbon-13 NMR
Spectra: A Collection of Assigned, Coded, and Indexed Spectra," by LeRoy F. Johnson and William
C. Jankowski, Wiley-Interscience, New York, 1972.

Figure 13.26 is courtesy of the National Institutes of Health.

Mass spectra are reproduced with permission from "EPA/NIH Mass Spectral Data Base," Supplement
I, S. R. Heller and G. W. A. Milne, National Bureau of Standards, 1980.

Figure 13.34 is adapted from R. Isaksson, J. Roschester, J. Sandstrom, and L.-G. Wistrand, *Journal of
the American Chemical Society*, 1985, 107, 4074-4075 with permission of the American Chemical
Society.

Figure 27.19 is adapted with permission from F. A. Quiocho and W. N. Lipscomb in "Advances in
Protein Chemistry," Volume 25, C. B. Anfinsen, Jr., J. T. Edsall, and F. M. Richards, Editors,
Academic Press, New York, NY, 1971.

Figure 27.22 is adapted with permission from Richard E. Dickerson in "The Proteins," second edition,
Volume II, H. Neurath, Editor, Academic Press, New York, NY, 1964.

2.4 CARBONYL-CONTAINING FUNCTIONAL GROUPS

Some of the most important families of organic compounds contain the **carbonyl group** (>C=O) and are listed in Table 2.2. Carbonyl-containing compounds are among the most abundant and biologically significant of naturally occurring substances, and the reactions of the carbonyl group feature prominently in *organic synthesis*—that branch of organic chemistry concerned with preparing a desired compound of defined structure by an appropriate sequence of reactions. Carbonyl-group chemistry is discussed in detail in Chapters 17 through 21.

2.5 INTRODUCTION TO ALKANES: METHANE

Alkanes are characterized by the general molecular formula $\text{C}_n\text{H}_{2n+2}$. The simplest alkane, methane, comprises a significant portion of the atmospheres of Jupiter, Saturn, Uranus, and Neptune. The atmospheres of these planets are said to be *reducing*. They are rich in hydrogen, and both nitrogen and carbon are found in their reduced forms, ammonia (NH_3) and methane (CH_4), respectively. Earth's weaker

TABLE 2.2
Classes of Compounds That Contain a Carbonyl Group

Class	Representative example	Name of example	Generalized abbreviation
Aldehyde	$\text{CH}_3\overset{\text{O}}{\parallel}\text{CH}$	Ethanal	$\text{RCH}\overset{\text{O}}{\parallel}$
Ketone	$\text{CH}_3\overset{\text{O}}{\parallel}\text{CCH}_3$	2-Propanone	$\text{RCR}\overset{\text{O}}{\parallel}$
Carboxylic acid	$\text{CH}_3\overset{\text{O}}{\parallel}\text{COH}$	Ethanoic acid	$\text{RCOH}\overset{\text{O}}{\parallel}$
Carboxylic acid derivatives:			
Acyl halide	$\text{CH}_3\overset{\text{O}}{\parallel}\text{CCl}$	Ethanoyl chloride	$\text{RCX}\overset{\text{O}}{\parallel}$
Acid anhydride	$\text{CH}_3\overset{\text{O}}{\parallel}\text{C}\overset{\text{O}}{\parallel}\text{CCH}_3$	Ethanoic anhydride	$\text{RCO}\overset{\text{O}}{\parallel}\text{C}\overset{\text{O}}{\parallel}\text{R}$
Ester	$\text{CH}_3\overset{\text{O}}{\parallel}\text{COCH}_2\text{CH}_3$	Ethyl ethanoate	$\text{RCOR}\overset{\text{O}}{\parallel}$
Amide	$\text{CH}_3\overset{\text{O}}{\parallel}\text{CNH}_2$	Ethanamide	$\text{RCNR}_2\overset{\text{O}}{\parallel}$

Alcohol dehydrogenase (Section 15.11): Enzyme in the liver which catalyzes the oxidation of alcohols to aldehydes and ketones.

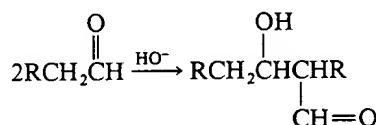
Aldaric acid (Section 25.19): Carbohydrate in which carboxylic acid functions are present at both ends of the chain. Aldaric acids are typically prepared by oxidation of aldoses with nitric acid.

Aldehyde (Section 17.1): Compound of the type RCH or ArCH .

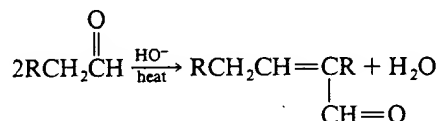
Alder rule (Section 10.13): The major stereoisomer formed in a Diels-Alder reaction is derived from the transition state in which the multiple bonds are closest to one another.

Alditol (Section 25.18): The polyol obtained on reduction of the carbonyl group of a carbohydrate.

Aldol addition (Section 18.8): Nucleophilic addition of an aldehyde or ketone enolate to the carbonyl group of an aldehyde or a ketone. The most typical case involves two molecules of an aldehyde, and is usually catalyzed by bases.



Aldol condensation (Sections 18.8–18.11): When an aldol addition is carried out so that the β -hydroxy aldehyde or ketone dehydrates under the conditions of its formation the product is described as arising by an aldol condensation.



Aldonic acid (Section 25.19): Carboxylic acid obtained by oxidation of the aldehyde function of an aldose.

Aldose (Section 25.1): Carbohydrate which contains an aldehyde carbonyl group in its open-chain form.

Alicyclic (Section 2.14): Term describing an *aliphatic cyclic* structural unit.

Aliphatic (Section 2.1): Term applied to compounds that do not contain benzene or benzenelike rings as structural units. (Historically, *aliphatic* was used to describe compounds derived from fats and oils.)

Alkadiene (Section 10.5): Hydrocarbon that contains two carbon-carbon double bonds; commonly referred to as a "diene."

Alkaloid (Section 22.5): Amine that occurs naturally in plants. The name derives from the fact that such compounds are weak bases.

Alkane (Section 2.1): Hydrocarbon in which all the bonds are single bonds. Alkanes have the general formula $\text{C}_n\text{H}_{2n+2}$.

Alkene (Section 2.1): Hydrocarbon that contains a carbon-carbon double bond ($\text{C}=\text{C}$); also known by the older name *olefin*.

Alkoxide ion (Section 4.8): Conjugate base of an alcohol; a species of the type $\text{R}-\ddot{\text{O}}:^-$.

Alkylamine (Section 22.1): Amine in which the organic groups attached to nitrogen are alkyl groups.

Alkylation (Section 9.7): Reaction in which an alkyl group is attached to some structural unit in a molecule.

Alkyl group (Section 2.12): Structural unit related to an alkane by replacing one of the hydrogens by a potential point of attachment to some other atom or group. The general symbol for an alkyl group is $\text{R}-$.

Alkyl halide (Section 4.1): Compound of the type RX , in which X is a halogen substituent (F , Cl , Br , I).

Alkylloxonium ion (Section 4.6): Positive ion of the type ROH_2^+ .

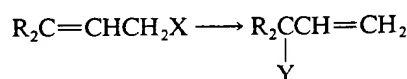
Alkyne (Section 2.1): Hydrocarbon that contains a carbon-carbon triple bond.

Allene (Section 10.5): The compound $\text{CH}_2=\text{C}=\text{CH}_2$.

Allyl cation (Section 10.2): The carbocation $\text{CH}_2=\text{CHCH}_2^+$. The carbocation is stabilized by delocalization of the π electrons of the double bond, and the positive charge is shared by the two CH_2 groups. Substituted analogs of allyl cation are called *allylic carbocations*.

Allyl group (Sections 5.1, 10.1): The group $\text{CH}_2=\text{CHCH}_2-$.

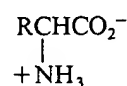
Allylic rearrangement (Section 10.2): Functional group transformation in which double bond migration has converted one allylic structural unit to another, as in:



Amide (Section 20.1): Compound of the type RCNR'_2 .

Amine (Chapter 22): Molecule in which a nitrogen-containing group of the type $-\text{NH}_2$, $-\text{NHR}$, or $-\text{NR}_2$ is attached to an alkyl or aryl group.

α -Amino acid (Section 27.1): A carboxylic acid that contains an amino group at the α -carbon atom. α -Amino acids are the building blocks of peptides and proteins. An α -amino acid normally exists as a *zwitterion*.



L-Amino acid (Section 27.2): A description of the stereo-

che
The
am
with

Amino
con

Amino
the
gro

Amylo
star

cose

amy
con

Amylo
of st

Anabol
mus

Androg
Angle s

beca
valu

Anion (C
Annule

acter
bond

Anomer
ranos

bony
bon t

Anti (Sec
subst

their l
struct

Anti addi
two p

posite

Antibond
in whi

an isol

Anticodon
molec

of mR